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Who should be really considered as a poor mobilizer in the plerixafor era?

Giovanna Andreola [a], Anna Vanazzi [b], Davide Radice [c], Aleksandra Babic [a], Cristina Rabascio [d], Mara Negri [a], Giovanni Martinelli [b], Daniele Laszlo [a,*]

[a] Stem Cell Collection Unit, European Institute of Oncology, Milan, Italy
[b] Division of Hematoncology, European Institute of Oncology, Milan, Italy
[c] Division of Statistics, European Institute of Oncology, Milan, Italy
[d] European Institute of Oncology, Laboratory of Haematoncology, 20141 Milan, Italy

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ABSTRACT

Patients with a number of peripheral CD34+ cells $\leqslant 20/\mu L$ have recently been defined in the literature as "poor mobilizers". We retrospectively reviewed medical records from a total of 248 patients affected by hematological malignancies or solid tumors undergoing peripheral blood stem cell collection following chemotherapy plus G-CSF. On the basis of the CD34+ cell peak in peripheral blood following mobilization therapy, patients were defined as good mobilizers (group A, CD34+ cells $\geqslant 20/\mu L$), relative poor mobilizers (group B, CD34+ cells <20 and $\geqslant 8/\mu L$) and absolute poor mobilizers (group C, CD34+ cells $<8/\mu L$). One hundred and seventy-seven (71%) patients resulted good mobilizers, 35 (14%) patients relative poor mobilizers and 36 (15%) patients absolute poor mobilizers. Target of stem cell collection was $\geqslant 2.0 \times 10^6$ CD34+ cells/kg for each transplantation procedure. All patients in group A, 20 patients in group B (57%) and 1 patient in group C (2.7%) were able to collect $\geqslant 2.0 \times 10^6$ CD34+ cells/kg. The multivariate analysis confirmed that more than three lines of previous chemotherapy and a previous autologous PBSC transplantation negatively affect mobilization of CD34+ cells in peripheral blood. Our data suggest that a number of CD34+ cells $\leqslant 20/\mu L$ does not always result in a failed stem cell collection and in fact in our patient series more than 70% of the patients defined as poor mobilizers have indeed collected the minimum number of 2.0×10^6 CD34+ cells/kg required for a successful transplantation. The use of new agent such as CXCR4 antagonist plerixafor might further improve mobilization efficacy in such patients.

1. Introduction

High dose chemotherapy followed by autologous peripheral blood stem cell (PBSC) transplantation represents a potentially curative treatment in hematological malignancies as well as in selected solid tumors [1–8]. Growth factors, mostly granulocyte colony stimulating factor (G-CSF), alone or in combination with chemotherapy are usually used to mobilize stem cells in peripheral blood which are then collected through one or more apheresis procedures. Generally, a collection of $\geqslant 2.0 \times 10^6$ CD34+ cells/kg is considered a minimum apheresis yield to achieve a safe engraftment after high dose chemotherapy; nevertheless a high proportion of patients, ranging from 11% to 40%, is reported in literature as unable to collect this target and is therefore considered "poor mobilizers" [9–15]. Age, underlying disease, disease status and bone marrow infiltration at the time of mobilization, previous lines of chemotherapy, prior use of fludarabine or radiotherapy are associated with a detrimental effect on stem cell mobilization, but definitive criteria to identify and predict patients who will not be able to collect an adequate amount of CD34+ cells are still lacking [9–11]. A peripheral number of 20 CD34+ cells/μL has been defined as the minimum to achieve a successful collection in most

* Corresponding author. Address: PBSC Collection Unit, European Institute of Oncology, Via Ripamonti 435, 20141 Milan, Italy. Tel.: +39 0257489538.
E-mail address: daniele.laszlo@ieo.it (D. Laszlo).

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Table 1
Patients characteristics according to circulating CD34+ cells.

		CD34 + (cells/μL)			Total	*p*-value[a]
		<8 *N* = 36 Group C	8–20 *N* = 35 Group B	⩾20 *N* = 177 Group A		
Sex	Male	17 (47.2)	22 (62.9)	101 (57.1)	140	0.395
	Female	19 (52.8)	13 (37.1)	76 (42.9)	108	
Previous CT Lines[b]	None	0	1 (2.9)	5 (2.8)	6	
	<3	17 (47.2)	22 (62.9)	156 (88.1)	195	***<0.001***
	⩾3	19 (52.8)	12 (34.3)	16 (9.0)	47	
Age (years)	<60	22 (77.8)	25 (71.4)	136 (76.8)	189	0.771
	⩾60	8 (22.2)	10 (28.6)	41 (23.2)	59	
^{90}Y Ibritumomab tiuxetan	No	31 (86.1)	35 (100)	176 (99.4)	242	***0.001***
	Yes	5 (13.9)	0	1 (0.6)	6	
Purine analogs	No	33 (91.7)	32 (91.4)	176 (99.4)	241	***0.004***
	Yes	3 (8.3)	3 (8.6)	1 (0.6)	7	
PEB	No	32 (88.9)	33 (94.3)	165 (93.2)	230	0.637
	Yes	4 (11.1)	2 (5.7)	12 (6.8)	18	
Radiotherapy	No	27 (75.0)	24 (68.6)	148 (83.6)	199	0.079
	Yes	9 (25.0)	11 (31.4)	29 (16.4)	49	
Previous transplantation	No	30 (83.3)	32 (91.4)	176 (99.4)	238	***<0.001***
	Yes	6 (16.7)	3 (8.6)	1 (0.6)	10	
Diagnosis[c]	HL	5 (13.9)	9 (25.7)	36 (20.3)	50	
	NHL	20 (55.6)	17 (48.6)	87 (49.2)	124	
	Leukemia	0	2 (5.7)	4 (2.3)	6	0.348
	MM	6 (16.7)	1 (2.9)	28 (15.8)	35	
	Solid tumor	5 (13.9)	6 (17.1)	22 (12.4)	33	
Mobilizing regimen	ESHAP-PEG	3 (8.3)	3 (8.7)	42 (23.7)	48	***0.023***
	Others	33 (91.7)	32 (91.4)	135 (76.3)	200	
	ESHAP-PEG[d]	3 (75.0)	3 (42.9)	42 (65.6)	48	0.581
	ESHAP-GCSF	1 (25.0)	4 (57.1)	22 (34.4)	27	

Abbreviation: CT, chemotherapy; HD, Hodgkin's Lymphoma; NHL, non-Hodgkin's Lymphoma; MM, multiple myeloma; ESHAP-PEG, CT according to ESHAP (see text) followed by pegylated G-CSF; ESHAP-G, CT according to ESHAP (see text) followed by G-CSF.
Bold italics numbers correspond to statistically significant values.
[a] Two-sided Fisher's exact test or Chi-square test where appropriate.
[b] Pairwise comparisons: <8 vs. 8–20, $p = 0.153$; <8 vs. ⩾20, $p < \mathbf{0.001}$; 8–20 vs. ⩾20, $p < \mathbf{0.001}$.
[c] p-value after excluding Leucemia: $p = 0.380$.
[d] Excluding other mobilizing regimens.

published studies; recently the consensus statement from the working group Gruppo Italiano Trapianto Midollo Osseo (GITMO) developed for patients affected by Lymphoma and Multiple Myeloma (MM), has officially defined as "poor mobilizers" those patients showing a peak of circulating CD34+ cells ⩽20/μL, for which the apheresis procedure might not be performed [9,10,16]. We retrospectively analyzed clinical records from 248 patients undergoing stem cell mobilization following chemotherapy and G-CSF to better define the group of "poor mobilizers" and the risk factors associated with a failed stem cell collection; this group of patients is in fact most likely to benefit from the use of new mobilizing agents (i.e. plerixafor) which have been recently marketed.

2. Patients and methods

2.1. Patients

From January 2006 to December 2010 a total of 248 patients underwent stem cell mobilization at our Institution. Patient's characteristics are summarized in Table 1. Median age was 51 years (range 18–77), 140 were male, 108 female; according to the REAL/WHO classification, 124 patients had a diagnosis of Non-Hodgkin's Lymphoma (60 Diffuse Large B Cell, 9 Peripheral T Cell, 27 Follicular, 24 Mantle Cell, 3 Marginal Lymphoma, 1 Waldenstrom Macroglobulinemia), 50 of Hodgkin's Lymphoma, 35 of MM, 5 of Acute Leukemia, 1 of Chronic Lymphocitic Leukemia; 33 patients had solid tumors. Median number of previous chemotherapy was 1 (range 1–9). Forty-seven patients had received ⩾3 prior chemotherapy regimens, 49 patients radiotherapy (RT), 6 patients radioimmunotherapy with ^{90}Y-Ibritumomab Tiuxetan (Zevalin®). Ten patients underwent mobilization after failing a previous autologous PBSC transplantation. Monolateral bone marrow biopsy revealed bone marrow disease infiltration in 46 (21%) patients affected by hematologic malignancies before mobilization.

2.2. Mobilizing regimens

In patients affected by hematologic disease the mobilization chemotherapy regimens were high-dose cyclofosfamide (4 g/ sq. m) followed by G-CSF (5 μg/kg, once daily), in 118 patients (47.5%), ESHAP (Etoposide 100 mg/sq. m for 3 days; cytosine arabinoside in two pulses each at a dose of 2 g sq. m given 12 h apart for 2 days; cisplatin 80 mg/sq. m on day 1; methylprednisolone 500 mg intravenously daily for 3 days) followed by G-CSF (5 μg/kg, once daily from day 4) in a total of 27 patients or followed by a single injection of pegylated G-CSF on day 4 in a total of 48 patients. Twenty-six patients affected by solid tumors